Doc Code: AP.PRE.REQ

PTO/SB/33 (07-05)
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U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

PRE-APPEAL BRIEF REQUEST FOR REVIEW	Docket Number (Optional) NEL-006

	Application Number	Filed
	10/091,567-Conf. #7851	March 7, 2002
	First Named Inventor: Jonathan P. Wong et al.	
	Art Unit: 1648	Examiner: M. G. Hill

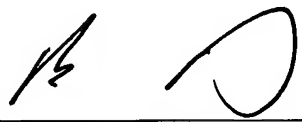
Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a notice of appeal.

The review is requested for the reason(s) stated on the attached sheet(s).
Note: No more than five (5) pages may be provided.

I am the

- [ ] applicant /inventor.
- [ ] assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96)
- [x] attorney or agent of record. Registration number 47,255
- [ ] attorney or agent acting under 37 CFR 1.34. Registration number if acting under 37 CFR 1.34. _____



Signature

Brian K. Dutton
Typed or printed name

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Telephone number

March 21, 2008
Date

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below*.

[x] *Total of 1 forms are submitted.

Docket No.: NEL-006
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Jonathan P. Wong et al.

Application No.: 10/091,567 | Confirmation No.: 7851

Filed: March 7, 2002 | Art Unit: 1648

For: DNA VACCINE USING LIPOSOME-ENCAPSULATED PLASMID DNA ENCODING FOR HEMAGGLUTININ PROTEIN OF INFLUENZA VIRUS | Examiner: M. G. Hill

REQUEST FOR PRE-APPEAL BRIEF PANEL REVIEW OF FINAL REJECTION

MS AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

This is a fully responsive amendment filed in response to the Final Office Action mailed September 21, 2007.

Claims 20-32 are pending. No new matter has been added.

An Amendment After Final Action (37 C.F.R. Section 1.116) has been filed on January 16, 2008 as a reply to the Final Office Action of September 21, 2007.

In view of this response, Applicants believe that all pending claims are in condition for allowance.

However, ***no response*** to the Amendment has been received.

Rejections under 35 U.S.C. §112 - Enablement

In the Final Office Action, the Examiner did not find Applicant's enablement arguments regarding "a plasmid encapsulated within a liposome" persuasive because of alleged ambiguities regarding the differences between complexes and liposome-encapsulated DNA. Applicant has amended the claims for clarification. Page 8 of the specification provides support for the amendment, wherein it explains that "Lipids, which are the basic components of liposomes, can entrap DNA molecules while forming a membrane vesicle-like structure." The method of making the liposome-encapsulated DNA is explained on pages 10-11 of the specification, and is readily understood by one of skill in the art. In this example, *cationic* liposomes were used for the encapsulation. [1]Since the claims require liposome-encapsulated DNA, one of skill in the art is able to practice the scope of the claims based upon the teachings of the disclosure. It is noted that liposome:plasmid DNA complexes are constructs that fall outside the scope of the claims.

Also, the Examiner objected to the language "long lasting" in claims 23 and 31 as not being enabled, alleging that the submitted evidence only demonstrated protection rather than "long lasting" protection. Applicant has amended the claims to eliminate the phrase.

As stated above, the disclosure and examples of the specification clearly demonstrate the effectiveness of the claimed method in preventing and/or treating influenza virus infection in humans. Thus, for these reasons, Applicants believe that this enablement rejection of claims 29-32 under 35 USC § 112, first paragraph, cannot be sustained and should be withdrawn.

Rejection under 35 U.S.C. §103

Claims 20-27 and 29-32 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Davis in view of Sha et al. and Promega Catalog. Claims 20 and 26-28 are further rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Wheeler et al, Webb et al., Yau-Young, and Davis et al. in view of Sha et al. Applicant respectfully traverses these rejections.

[1] Additionally, clarification is sought from the Examiner regarding the statement that "anionic charged lipids will surround the plasmid as they form complexes to cover the negatively charged DNA." This statement appears to be incorrect.

To establish a *prima facie* case of obviousness, the cited references, in combination, must teach or suggest the invention as a whole, including all the limitations of the claims. MPEP § 2142. Here the combination of (1) Davis et al. Sha et al. and Promega Catalog, and (2) Wheeler et al., Webb et al., Davis et al. and Sha et al., fails to teach the claimed liposomal vaccine composition (i.e. **liposome-encapsulated plasmid DNA** *wherein the liposome is prepared from a cationic lipid film which is mixed with a solution containing said plasmid*) and the method of making thereof.

As previously argued, Applicants submit that there is no motivation to modify or combine the teaching of the cited references. Under U.S. practice, to establish a *prima facie* case of obviousness, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify or combine reference teachings. As noted in Applicant's earlier responses and arguments which the Examiner had found persuasive, a novel and unobvious aspect of the patent invention is that the DNA vaccine is encapsulated within the liposomes, and not complexed with the lipids. Since the application of the Webb et al. reference is for increasing the circulation time and the pharmacokinetics of the anticancer drug, vinersitine (see abstract, page 272, line 6-9, of Webb et al.) in the body and not about encapsulating plasmid DNA vaccine within liposomes, and avoiding DNA-lipocomplex formation, Applicant submits that there is insufficient motivation in the cited references to modify or combine reference teachings.

Further, Davis et al. only contains a general discussion on the use of plasmid DNA vaccines as a *background* to Davis's CpG oligos technology. Davis teaches the use of nucleic acids containing unmethylated CpG dinucleotide as an adjuvant. The unmethylated CpG dinucleotide is not a plasmid, and an adjuvant is not a vaccine. Rather, adjuvants such as CpG oligos are compounds that could be used to enhance the immune responses to vaccines. The broad and generic teachings of Davis are not sufficient to not obviate the distinctive liposome-encapsulated plasmid DNA of the pending claims.

The citation in Davis et al. noted by the Examiner (see column 26, lines 15-50, of Davis et al.) only discusses liposomes as a possible delivery system but does not at all disclose encapsulating plasmid DNA vaccine within liposomes. Applicant respectfully requests that the

Examiner provide a citation as to where in Davis et al. does it disclose or teach encapsulating plasmid DNA vaccine within liposomes.

It should also be noted that Davis et al. primarily focuses on the use of CpG oligos to enhance the immune responses to hepatitis B vaccine (HBV) which is in conflict with the present invention which does not advocate using CpG oligos or developing an adjuvant to Hepatitis virus vaccine. Hence, it is clear that Davis et al. teaches away from the present invention since one skilled in the art would not be motivated to modify the teachings of Davis et al. to arrive at the present invention. Under U.S. case law, a prior art reference that "teaches away" from the claimed invention is a significant factor to be considered in determining obviousness. In other words, it is improper to combine references where the references teach away from their combination. *In re Grasselli*, 713 F.2d 731, 743, 218 USPQ 769, 779 (Fed. Cir. 1983).

In addition, there is a significant difference between generating an antibody response to a vaccine (Davis et al.) and viral infection protection, because high antibody response does not guarantee protection against virus infections. In other words, it is well known in the art that antigens generating good antibody response are found to be ineffective when tested for efficacy against a real virus challenge in animals and humans. Therefore, modification of the teachings in Davis et al. does not provide a reasonable expectation of success, as required to establish a *prima facie* case of obviousness.

Lastly, in further support of Applicant's position that the prior art references are not in the Applicant's field of endeavor, and are not reasonably pertinent to the particular problem with which the Applicant was concerned, Applicant submits that the endeavour and particular problem being applied in the present application is vaccine development against infectious diseases while, for example, Webb et al, relates to oncology and cancer therapy. Webb discloses ceramides together with polyethylene glycol as a lipid component for liposomes with that support transfection in target cells for gene expression. By contrast, Webb does not suggest or teach liposome encapsulation for DNA vaccine development. Importantly, the liposome encapsulation of the plasmid DNA supports the longer half-life of the vaccine, which is more efficacious than DOSPER complexed plasmid vaccines. In fact, given the differences in encapsulating DNA vaccine versus

anticancer drug, Applicant does not believe that the problems and solutions of encapsulating an anticancer drug would relate to the problems associated with encapsulating a DNA vaccine.

Thus, for these reasons, withdrawal of this rejection is respectfully requested.

Conclusion

For the foregoing reasons, all the claims now pending in the present application are allowable, and the present application is in condition for allowance.

Therefore, this response is believed to be a complete response to the Office Action.

Applicants reserve the right to set forth further arguments supporting the patentability of their claims, including the separate patentability of the dependent claims not explicitly addressed herein, in future papers.

There is no concession as to the veracity of Official Notice, if taken in any Office Action. An affidavit or document should be provided in support of any Official Notice taken. 37 CFR 1.104(d)(2), MPEP § 2144.03. See also, *Ex parte Natale*, 11 USPQ2d 1222, 1227-1228 (Bd. Pat. App. & Int. 1989)(failure to provide any objective evidence to support the challenged use of Official Notice constitutes clear and reversible error).

Accordingly, favorable reexamination and reconsideration of the application in light of the remarks is courteously solicited.

Dated: March 21, 2008

Respectfully submitted,

By _____

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